LETTER

A clinical specification for a randomized clinical trial on lithium in amyotrophic lateral sclerosis

We read with great interest the paper by Fornai *et al*. (1) on delayed progression of amyotrophic lateral sclerosis (ALS) with lithium. In this study the results of a small randomized clinical trial were also reported. Sixteen patients (4 of whom had the bulbar form of ALS) were randomly selected to receive riluzole plus lithium, and 28 (7 of whom had the bulbar form of ALS) received riluzole only. At the end of the follow-up (15 months) all 16 patients treated with lithium and riluzole were alive, whereas 8 of 28 treated only with riluzole died (the survival rate was 100% vs. 71%). Moreover, secondary outcomes, measuring changes in global function of ALS patients by means of ALSFRS-R (revised ALS Functional Rating Scale) and Norris ALS scales, and disease progression with more objective measures, such as the Medical Research Scale and pulmonary function (forced vital capacity), were reported. At the end of the study, all of these secondary end points were more favorable for the lithium-treated patients with respect to the other patients' group. We ask the authors about the clinical form of ALS of the eight patients deceased.

We believe that now a larger randomized clinical trial should be conducted to confirm these very interesting results reported by Fornai *et al*. (1). We suggest that in this context a sequential trial design should be adopted. This is an alternative method to the classical trial design, which permits stopping a study as soon as a treatment effect can be significantly demonstrated or denied (2).

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1. Fornai F, *et al.* (2008) Lithium delays progression of amyotrophic lateral sclerosis. *Proc Natl Acad Sci USA* 105:2052–2057.
2. Groeneveld GJ, Graf M, van der Tweel I, van den Berg LH, Ludolph AC (2007) Alternative trial design in amyotrophic lateral sclerosis saves time and patients. *Amyotroph Lateral Scler* 8:266–269.

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The authors declare no conflict of interest.

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